Technology and Mechanisms of transcranial Direct Current Stimulation

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Disclosure:

Soterix Medical Inc. produces tDCS and High-Definition tDCS. Marom Bikson is founder and has shares in Soterix Medical. Some of the clinical data presented may be supported by Soterix Medical.
Transcranial Direct Current Stimulation (tDCS)

- Non-invasive, portable, well-tolerated neuromodulation.
- Low-intensity (~2 mA) current passed between scalp electrodes (~20 min).
- Investigated for cognitive neuroscience and neuropsychiatric treatment.

Depression, pain, migraine, epilepsy, PTSD, schizophrenia, tinnitus, neglect, rehabilitation (motor, aphasia), TBI, OCD, attention, Accelerated learning (reading, motor skills, math, threat detection), memory...

- Can a “simple” intervention modulate brain function?
- How is specificity of action achieved?
Neuromodulation: Electrotherapy Delivery Platforms

Deep Brain Stimulation (invasive)  
Transcranial Magnetic Stimulation  
transcranial Direct Current Stimulation

Decreasing Cost
- Deployable, compact
- Minimal supervision
- Adverse events: itching, erythema
- IRB / FDA “NSR”

Decreasing Risk

Increasing Efficacy, Specificity

? tDCS Specificity
What makes tDCS specific?

Given the diversity of tDCS application spanning neuropsychiatric treatment, rehabilitation, and learning in healthy individuals.

- **Anatomical targeting (specificity)**
  The control of tDCS Dose (Peterchev Brain Stim 2013) electrode placement to produce current flow in targeted brain regions.
  Design facilitated by current flow models.

- **Functional targeting (specificity)**
  The use of tDCS *adjunct* to behavioral / cognitive training to facilitate the outcomes of training.
  Design facilitated by quantitative descriptions (cellular models) developed using animal experiments.
Anatomical targeting with tDCS

- “Conventional” tDCS varies the position of two large electrodes.
- Montage specific effects on behavior and neurophysiology well documented.
- “Shaping” outcomes vs “targeting” brain regions.
Anatomical targeting with tDCS

Datta et al. Brain Stim 2009

High-Definition electrodes in “4x1” configuration

Conventional bipolar large electrodes
High-Definition electrodes in “4x1” configuration

Datta et. al. Brain Stim 2009

Optimized tDCS is a “closed” problem

But “best” montage different for:

a) Maximum **intensity** at target.

b) **Focality** (minimizing relative intensity outside of target).

Dmochowski Neural Engr. 2011
Customized targeting with tDCS

Super-obese
Obesity / Craving / Addiction

Pediatric
Epilepsy / ADHD / CP

Stroke
Rehabilitation (motor, aphasia)

Kessler PLoS ONE 2013
Gillick Frontiers 2014

Truong Neuroimage 2013
Datta Brain Stimulation 2011
Dmochowski Neuroimage 2013
tDCS mechanisms: Neuromodulation

High-intensity Pulses

Low-intensity DC

Over-driving a neural network

Neuromodulation comes from secondary non-linear changes

Deep Brain Stimulation

Motor Cortex Stimulation

Transcranial Magnetic Stimulation (TMS)
tDCS mechanisms: Neuromodulation

High-intensity Pulses

Over-driving a neural network

Low-intensity DC
tDCS mechanisms: Neuromodulation

High-intensity Pulses

Over-driving a neural network

Low-intensity DC

Neuromodulation
tDCS mechanisms: Neuromodulation

High-intensity Pulses

Over-driving a neural network

Low-intensity DC

Interacting with specific activity in a neural network (Neuromodulation)

Transcranial Direct Current Stimulation (tDCS)
Anatomical targeting with brain stimulation

Supra-threshold stimulation

DBS M1s TMS


Sub-threshold stimulation

HD-tDCS 4x1

Stimulation primary neuromodulation target. Endogenous circuit.

• “Quasi-Uniform” assumption: Neuromodulation is linear with local electric field magnitude.

Bikson Brain Stim 2010
From Anatomical Targeting to Functional Targeting

- Network of interest (e.g. depression, math cells)
- Other networks – not targets for neuromodulation

Electrode / Coil

Preferential modulation of more active network (activity dependent)

Current flow across entire region

Network of interest (e.g. depression, math cells)
What makes tDCS specific?

“Given” the diversity of tDCS application spanning neuropsychiatric treatment, rehabilitation, and learning in healthy individuals:

• **Anatomical targeting (specificity)**
  The control of tDCS Dose (Peterchev Brain Stim 2013) through coil / electrode placement to produce current flow in targeted brain regions. 
  Design facilitated by current flow models.

• **Functional targeting (specificity)**
  The use of tDCS *adjunct* to behavioral / cognitive training to facilitate the outcomes of training. 
  Design facilitated by quantitative descriptions (cellular models) developed using animal experiments.
**Functional specificity of tDCS**

**Preferential neuromodulation of “ongoing” activity**

**Cellular Level:**
- DCS produces linear membrane polarization leading to cumulative (with endogenous activity) changes neuronal firing.
  
  Radman Brain Stim 2009

**Synaptic Level:**
- DCS modulates synaptic efficacy and plasticity of active pathways (e.g. boosts ongoing plasticity).
  
  Bikson J Physiol 2004

**Network Level:**
- DCS modulates ongoing oscillations.
- Nature of modulation entirely determined by network dynamics.
  
  Reato J Neurosci 2010

“More” active systems are modulated “more” by DCS
Rational tDCS Clinical Trials: Specificity

- Phase-2 Harvard/Spaulding (Fregni, Geva): Fibromyalgia ongoing
- End-point 50% reduction in pain: Adaptive therapy
- Soterix Medical HD-tDCS
- **thermode** (pain evoked potential) -> *Elminda* EEG
- Principle of both anatomical and functional targeting
- End-point met in 5 of (5 + 4 dropouts)
  - All electrographic responders
- Data-base (“cloud”) on brain response
  - Informs future treatment
- Molecular (u-opiod) imaging (DaSilva)

- Can a “simple” intervention modulate brain function?
- How is specificity of action achieved?
Deployable tDCS (keeping is simple)

- Repeated sessions (e.g., weeks) required for efficacy and maintenance.
- Home-based therapy reduces burden on patients (travel) and hospital (cost).
- “Home” technology focused on compliance.
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